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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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EXAMINER

SWOPE, SHERIDAN

ART UNIT PAPER NUMBER

1652

DATE MAILED: 09/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/696,070

Applicant(s)

ROTHMAN ET AL.

Examiner

Sheridan L. Swope

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14-19 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 14-19 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Applicant's cancellation of Claims 1-13 and 20-43 and amendment of Claims 14-19 in Paper No. 3 is acknowledged. Claims 14-19 are pending and are hereby examined.

Claim Rejections - 35 USC § 112-First Paragraph

Claims 14-19 are rejected under 35 U.S.C. 112, first paragraph. The specification is enabling for the polynucleotides of SEQ ID NO: 14, 16, 18, 20, 22, 24, 26, 28, 30, and 35 as well as polynucleotides encoding the proteins set forth in SEQ ID NO: 13, 15, 17, 19, 21, 23, 25, 27, 29, and 34. However, the specification does not reasonably provide enablement for all polynucleotide sequences encoding the KDELr (KDELr) inhibitors recited in Claims 14-19. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 14 is so broad as to encompass any polynucleotide sequence that encodes any KDELr inhibitor comprising any trimer of subunits, wherein each subunit comprises any oligomerization domain and any region, at its C-terminus, which binds to any KDELr. This claim is not enabled in three ways. First, it is not enabled for any combination of any three subunits. Second, it is not enabled for any oligomerization domain. Third, it is not enabled for any region that binds to any KDELr. Claims 15-19 are also not enabled for any polynucleotide encoding any KDELr inhibitor comprising any trimer of subunits. Claims 16, 18, and 19 are also not enabled for any polynucleotide encoding any KDELr inhibitor in which each subunit has, at its C-terminus, any region that binds to any KDELr. Claim 15 is also not enabled for any polynucleotide encoding any KDELr inhibitor in which each subunit has any oligomerization

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domain. Claims 16 and 17 are also not enabled for any polynucleotide encoding any KDELR inhibitor in which each subunit has any pentamerization domain. Claims 18 and 19 are also not enabled for any polynucleotide encoding any KDELR inhibitor in which each subunit has any pentamerization domain, wherein the pentamerization domain is derived from a any cartilage oligomeric matrix protein. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired KDELR inhibitor activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the amino acid sequences of SEQ ID NO: 13, 15, 17, 19, 21, 23, 25, 27, 29, and 34 and the nucleotide sequences of SEQ ID NO: 14, 16, 18, 20, 22, 24, 26, 28, 30, and 35.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

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The specification does not support the broad scope of:

Claims 14-19 which, encompasses all polynucleotide sequences that encode a protein having KDELr inhibitor activity and having any trimer of subunits.

Claims 16, 18, and 19 which, encompasses all polynucleotide sequences that encode a protein having KDELr inhibitor activity in which, each subunit has any region that binds to any KDELr.

Claim 15 which, encompasses all polynucleotide sequences that encode a protein having KDELr inhibitor activity in which, each subunit has any oligomerization domain.

Claims 16 and 17 which, encompasses all polynucleotide sequences that encode a protein having KDELr inhibitor activity in which, each subunit has any pentamerization domain.

Claims 18 and 19 which, encompasses all polynucleotide sequences that encode a protein having KDELr inhibitor activity in which, each subunit has any pentamerization domain, wherein the pentamerization domain is derived from any cartilage oligomeric matrix protein.

The specification does not support the broad scope of Claims 14-19 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting the activity of the KDELr inhibitors; (B) the general tolerance of the activity of the KDELr inhibitors to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope

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of the claims broadly including any number of KDELr inhibitors with an enormous number of amino acid modifications of the KDELr inhibitors of SEQ ID NO: 13, 15, 17, 19, 21, 23, 25, 27, 29, and 34. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of polynucleotide sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 14-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of DNA molecules encoding any KDELr inhibitor from any source. The specification teaches the structure of only ten representative species of such DNAs. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding a KDELr inhibitor. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 16-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the


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art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 16-19 recite a genus of KDELr inhibitors comprising a trimer of protein subunits wherein each subunit comprises a pentamerization domain. The specification does not provide enablement for any KDELr inhibitors comprising a trimer of protein subunits wherein each subunit comprises a pentamerization domain. Thus, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention as recited in these claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 703-305-1696. The examiner can normally be reached on M-F; 8:30-5 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


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